Calcium Phosphate, Dibasic Dihydrate

1 Nonproprietary Names

BP: Calcium Hydrogen Phosphate Dihydrate
JP: Dibasic Calcium Phosphate Hydrate
PhEur: Calcium Hydrogen Phosphate Dihydrate
USP–NF: Dibasic Calcium Phosphate Dihydrate

2 Synonyms

Calcii hydrogenophosphas dihydricus; calcium hydrogen orthophosphate dihydrate; calcium monohydrogen phosphate dihydrate; *DI-CAFOS D*; dicalcium orthophosphate; *DI-TAB*; E341; *Emcompress*; phosphoric acid calcium salt (1:1) dihydrate; secondary calcium phosphate.

3 Chemical Name and CAS Registry Number

Dibasic calcium phosphate dihydrate [7789-77-7]

4 Empirical Formula and Molecular Weight

$CaHPO_4 \cdot 2H_2O$ 172.09

5 Structural Formula

See Section 4.

6 Functional Category

Tablet and capsule diluent.

7 Applications in Pharmaceutical Formulation or Technology

Dibasic calcium phosphate dihydrate is widely used in tablet formulations both as an excipient and as a source of calcium and phosphorus in nutritional supplements.[1–8] It is one of the more widely used materials, particularly in the nutritional/health food sectors. It is also used in pharmaceutical products because of its compaction properties, and the good flow properties of the coarse-grade material. The predominant deformation mechanism of dibasic calcium phosphate coarse-grade is brittle fracture and this reduces the strain-rate sensitivity of the material, thus allowing easier transition from the laboratory to production scale. However, dibasic calcium phosphate dihydrate is abrasive and a lubricant is required for tableting, for example about 1% w/w of magnesium stearate or about 1% w/w of sodium stearyl fumarate is commonly used.

Two main particle-size grades of dibasic calcium phosphate dihydrate are used in the pharmaceutical industry. The milled material is typically used in wet-granulated, roller-compacted or slugged formulations. The 'unmilled' or coarse-grade material is typically used in direct-compression formulations.

Dibasic calcium phosphate dihydrate is nonhygroscopic and stable at room temperature. However, under certain conditions of temperature and humidity, it can lose water of crystallization below 100°C. This has implications for certain types of packaging and aqueous film coating since the loss of water of crystallization appears to be initiated by high humidity and by implication high moisture vapor concentrations in the vicinity of the dibasic calcium phosphate dihydrate particles.[8]

Dibasic calcium phosphate dihydrate is also used in toothpaste and dentifrice formulations for its abrasive properties.

Table I: Pharmacopeial specifications for calcium phosphate, dibasic dihydrate.

Test	JP XVII	PhEur 9.2	USP 40–NF 35 S1
Identification	+	+	+
Characters	+	+	—
Loss on ignition	24.5–26.5%	24.5–26.5%	24.5–26.5%
Acid-insoluble substances	≤0.2%	≤0.2%	≤0.2%
Heavy metals[a]	≤31 ppm	—	≤30 ppm
Chloride	≤0.25%	≤0.25%	≤0.25%
Fluoride	—	≤100 ppm	≤50 ppm
Sulfate	≤0.48%	≤0.5%	≤0.5%
Carbonate	+	+	+
Barium	+	+	+
Arsenic	≤2 ppm	≤10 ppm	≤3 µg/g
Iron	—	≤400 ppm	—
Assay	98.0–105.0%	98.0–105.0%	98.0–105.0%

(a) These tests have not been fully harmonized at the time of publication.

8 Description

Dibasic calcium phosphate dihydrate is a white, odorless, tasteless powder or crystalline solid. It occurs as monoclinic crystals.

9 Pharmacopeial Specifications

The pharmacopeial specifications for dibasic calcium phosphate dihydrate have undergone harmonization of many attributes for JP, PhEur, and USP–NF.

See Table I. *See also* Section 18.

10 Typical Properties

Acidity/alkalinity pH = 7.4 (20% slurry of *DI-TAB*)
Angle of repose 28.3° for *Emcompress*.[9]
Density (bulk) 0.915 g/cm^3
Density (tapped) 1.17 g/cm^3
Density (true) 2.389 g/cm^3
Flowability 27.3 g/s for *DI-TAB*;11.4 g/s for *Emcompress*.[9]
Melting point Dehydrates below 100°C.
Moisture content Dibasic calcium phosphate dihydrate contains two molecules of water of crystallization, which can be lost at temperatures well below 100°C.
Particle size distribution *DI-TAB*: average particle diameter 180 µm; fine powder: average particle diameter 9 µm.
Solubility Practically insoluble in ethanol, ether, and water; soluble in dilute acids.
Specific surface area 0.44–0.46 m^2/g for *Emcompress*.
Spectroscopy

IR spectrum *see* Figure 1.

NIR spectrum *see* Figure 2.

Raman spectrum *see* Figure 3.

11 Stability and Storage Conditions

Dibasic calcium phosphate dihydrate is a nonhygroscopic, relatively stable material. However, under certain conditions the dihydrate can lose water of crystallization. This has implications for both storage of the bulk material and coating and packaging of tablets containing dibasic calcium phosphate dihydrate.

The bulk material should be stored in a well-closed container in a cool, dry place.